REMARKS/ARGUMENTS

Claims 18, 21-25, 37, 39-43, and 54 are pending. Claims 19, 20, 26-36, 38, 44 and 55-68 have been withdrawn from consideration. Claims 69-74 are new. Claims 18 and 37 have been amended to further describe the hybridization conditions. Support for this amendment is found in the specification at page 7, line 24-*et seq*. Support for new Claim 69 is found in original Claim 37. Claims 70-74 present limitations already found in Claim 18. Other amendments have been made to improve the clarity of the claims. Accordingly, the Applicants do not believe that any new matter has been added.

Restriction/Election

The Restriction Requirement has now been made FINAL. The non-elected claims have been revised to facilitate possible rejoinder and the Applicants respectfully request that the claims of the nonelected groups which depend from or include all the limitations of those of Group I, be rejoined upon an indication of allowability for the elected claims, see MPEP 821.

Priority

To clarify the record, the Applicants note that the current application was filed on June 27, 2002 and is a national-stage filing under §371 of PCT/JP00/04515, filed on July 6, 2000, which in turn claims priority to provisional application 60/159,586, filed on October 18, 1999, and foreign application JP11-194179 filed on July 8,1999.

Rejection--35 U.S.C. § 112, second paragraph

Claims 18, 24, 25, 37, 42, and 43 were rejected under 35 USC 112, second paragraph, as being indefinite. These rejections are moot in view of the amendments above.

Rejection--35 U.S.C. § 112, first paragraph

Claims 18, 21-25, 37, 39-43 and 54 were rejected for lack of written description and enablement. The Official Action rejects these claims on three bases: (1) the claimed polynucleotides include the term "functional equivalents", (2) the claimed polynucleotides hybridize to SEQ ID NOs: 1, 3, 5, 7 or 9 under conditions less stringent than 0.1X SSC, 0.1 % SDS, 65°C, and (3) the claimed polynucleotides have less than 95% identity to SEQ ID NOs: 1, 3, 5, 7 or 9 of less than 95%.

Each of these concerns has been addressed by the above amendment. (1) The claims have been revised to delete the term "functional equivalents"; (2) Claims 18 and 37 have been revised to more clearly describe the claimed hybridization conditions by reference to washing in 0.1X SSC, 0.1% SDS, at 65°C; and (3) Claims 18 and 37 require that the protein contain no more than 5% mutations. Also, the overall percent identity is now required to be at least 95%. The specification discloses DNAs that encode proteins comprising the amino acid sequences of SEQ ID NOs: 4, 6, 8 or 10 and discloses methods for obtaining these DNAs by hybridization or PCR (page 4, line 33 to page 5, line 1).

> One skilled in the art would be able to prepare proteins functionally equivalent to the proteins used in the β-amyloid aggregation tests described in the working examples below, for example, by using a method for introducing mutations into the amino acid sequences of proteins (e.g. site-directed mutagenesis, Current Protocols in Molecular Biology edit. Ausubel et al. (1987) Publish. John Wily & Sons Section 8.1-8.5). Such proteins might occur due to spontaneous mutation of amino acids in nature. The present invention also includes a protein having an amino acid sequence in which one or several amino acid residues are different from those found in a sequence of any one of the proteins identified in the working examples below (SEQ ID NO. 2, 4, 6, 8 or 10, or the amino acid sequence encoded by SEQ ID NO. 1, 3, 5, 7 or 9) due to a substitution, deletion, insertion and/or addition, as long as the

protein retains a function equivalent to the proteins identified in the working examples below.

Furthermore, the specification discloses methods for producing recombinant proteins using expression vectors (page 8, line 30 to page 10, line 31). The specification discloses methods for determining whether or not a protein has the required functional activity of suppressing or promoting aggregation of amyloid (page 30, line 1 to page 31, line 12). Moreover, methods for introducing mutations, such as site-directed mutagenesis, were well known in the art prior to the priority date of the present application. Accordingly, the Applicants respectfully request that this rejection now be withdrawn.

Claim rejections, 35 U.S.C. § 101

Claims 18, 21-25, 37, 39-43 and 54 were rejected under 35 U.S.C. 101 for lack of utility. The Applicants thank the Examiner for acknowledging the utility of proteins encoded by SEQ ID NOs: 1, 3 and 7 since they suppress the aggregation or deposition of Aβ, which makes them useful at least to treat Alzheimer's disease.

The rejection suggests that the proteins encoded by SEQ ID NOs: 5 and 9 promote aggregation or deposition of Aβ and thus lack utility because promotion of aggregation would have deleterious effects. The Applicants respectfully disagree because such proteins are useful for modeling diseases like Alzheimer's disease and are also useful in diagnostic methods. As described in page 15, line 34 to page 16, line 4 of the specification, proteins encoded by the polynucleotides of SEQ ID NOs: 5 and 9 comprise the activity of enhancing amyloid-β protein aggregation, and their expression increases in patients with Alzheimer's disease. Therefore, reducing the expression level of these proteins will prevent amyloid-β protein aggregation, and thus, will be useful for treating and preventing Alzheimer's disease. For example, these proteins are useful for assaying or screening therapeutic agents that suppress the aggregation of amyloid-β and such a screening method is described in the

specification (page 15, line 18 to 26). In addition, the polynucleotides of SEQ ID NOs. 5 and 9 are useful for producing animal models of Alzheimer's disease. Since their expression increases in patients with Alzheimer's disease, the polynucleotides of SEQ ID NOs: 5 and 9 and proteins encoded thereby are also useful for detecting Alzheimer's disease. Such detection methods are described on page 24, line 11 to page 25, line 10 of the specification. Accordingly, the polynucleotides of SEQ ID NOs. 5 and 9, and proteins encoded thereby, have patentable utilities.

Rejections, 35 U.S.C. § 102 and §103

Claims 18, 21, 37, 39 and 54 were rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al. (WO98/21328) and Claims 18, 21-25, 37, 39-43 and 54 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al. (WO98/21328).

Kato is directed to a polynucleotide that is 99.7% identical to SEQ ID NO: 1.

These rejections are moot in view of the deletion of SEQ ID NO: 1 and SEQ ID NO: 2 from the claims.

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application is in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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